

204070-4540400T

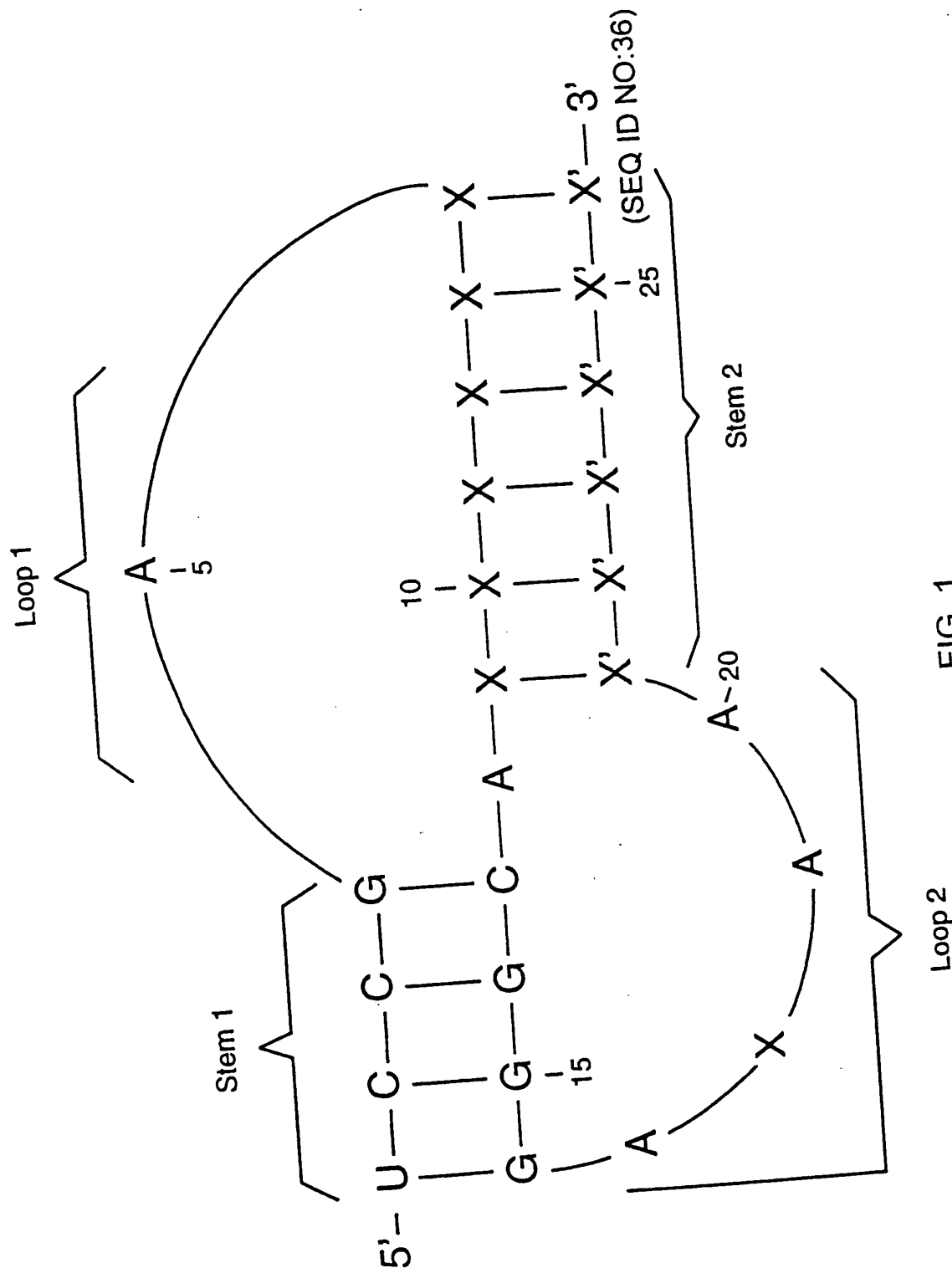


FIG. 1

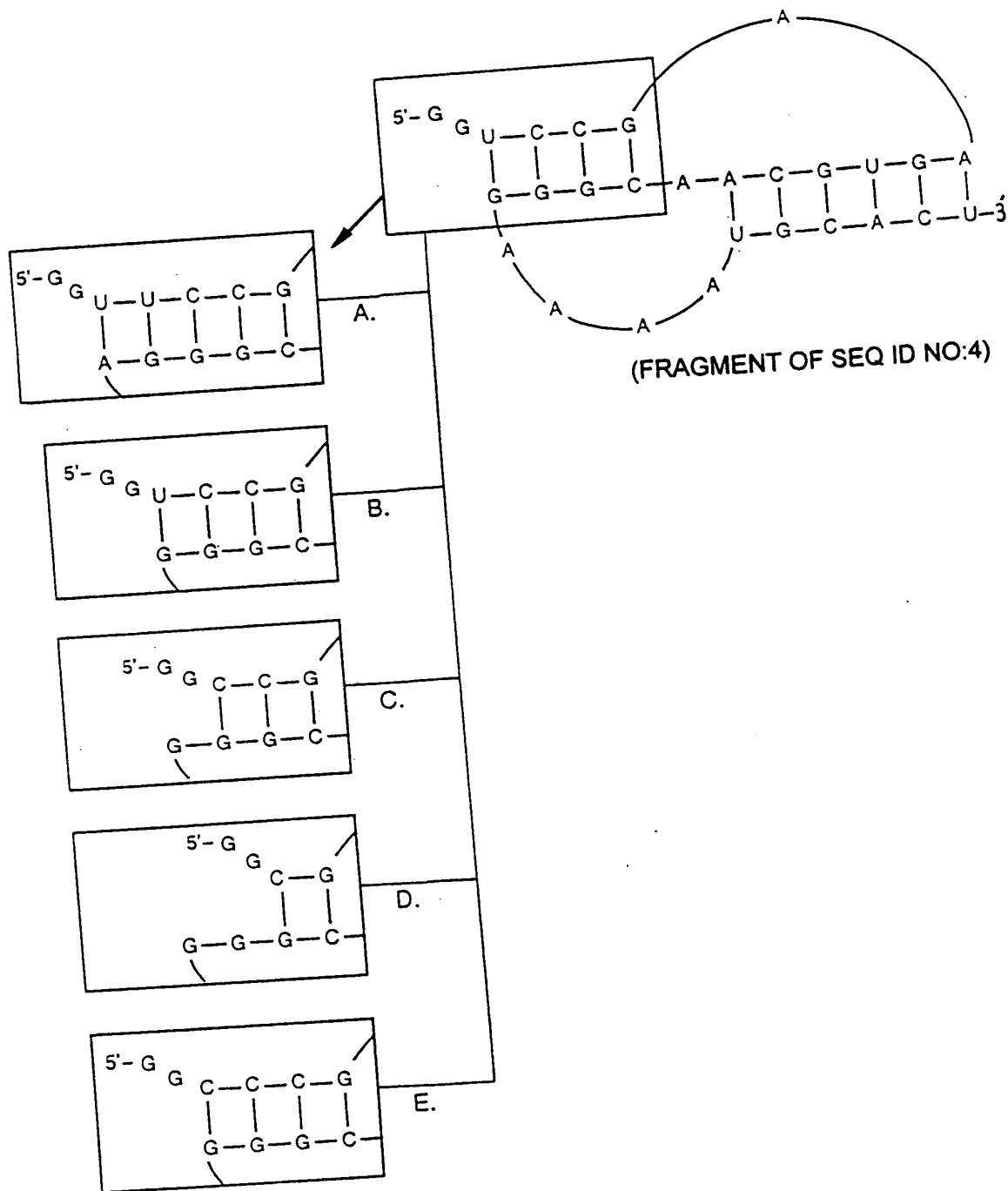


FIG. 2A

10040497.010702

202010-260400T

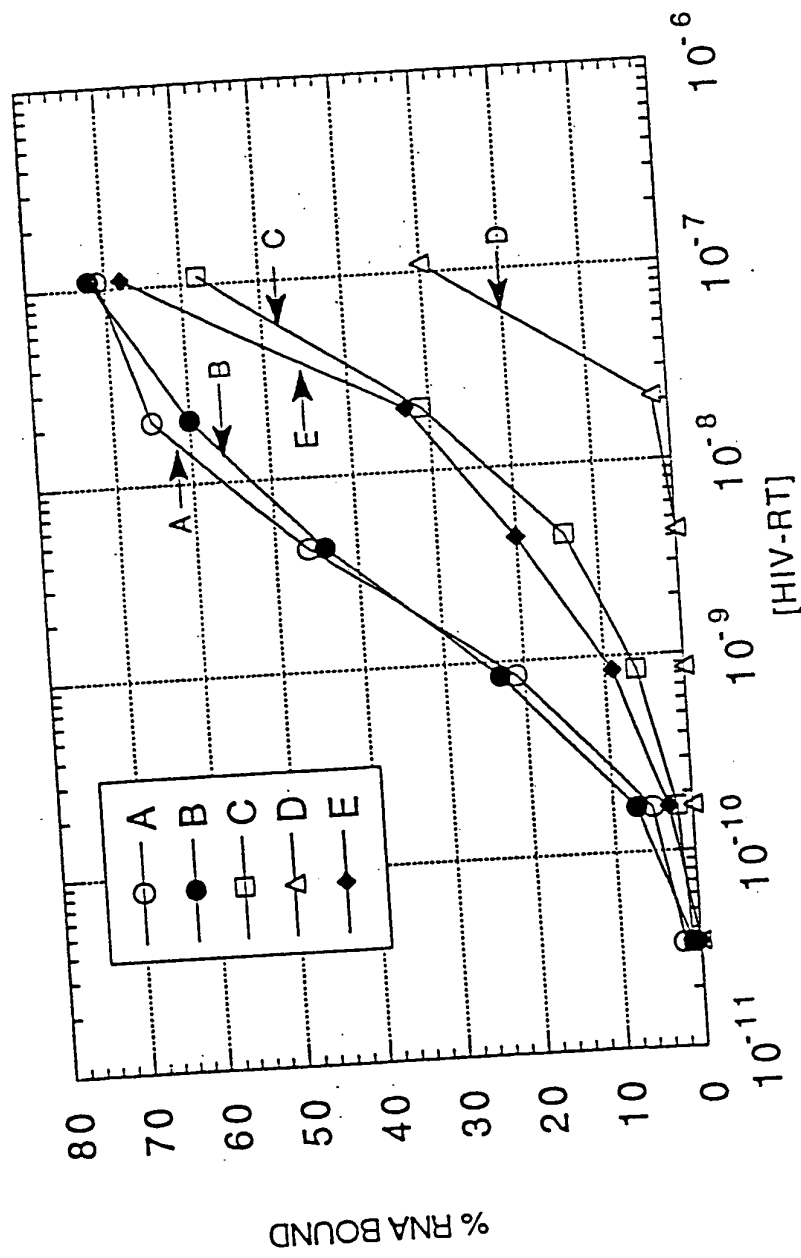


FIG.2B

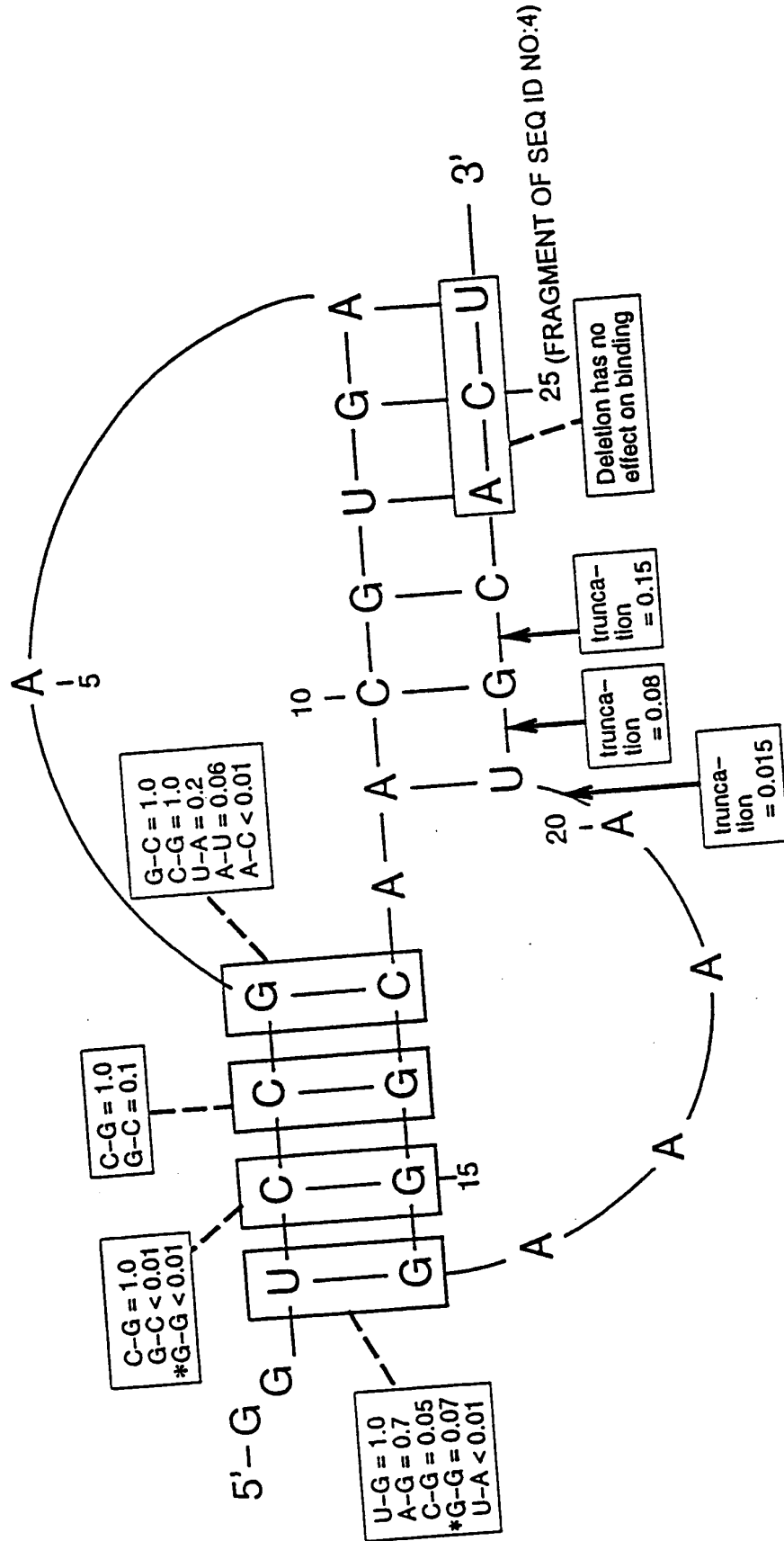


FIG. 3

204010" 2640400T

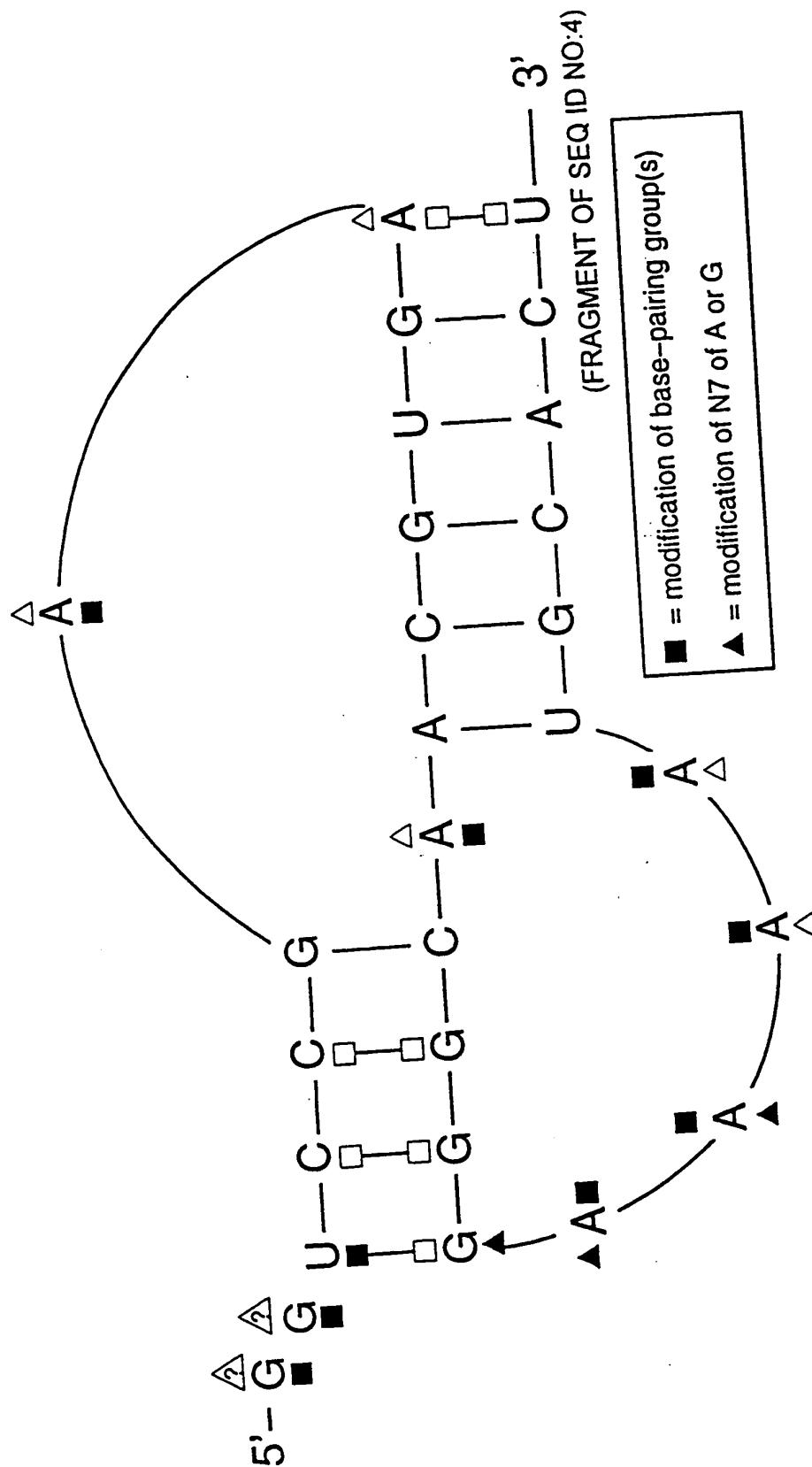
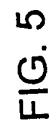


FIG. 4



202070" 2640400F

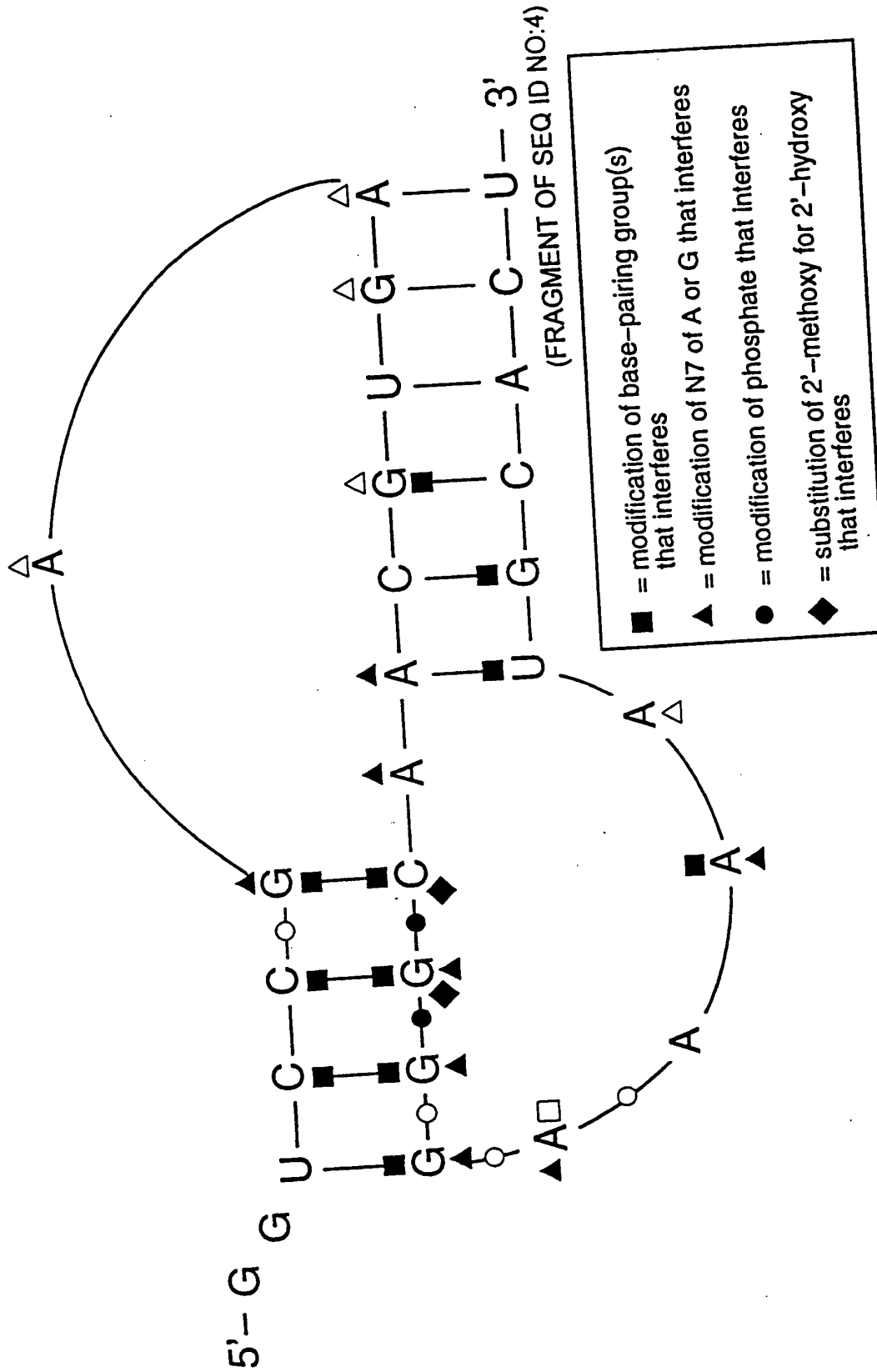
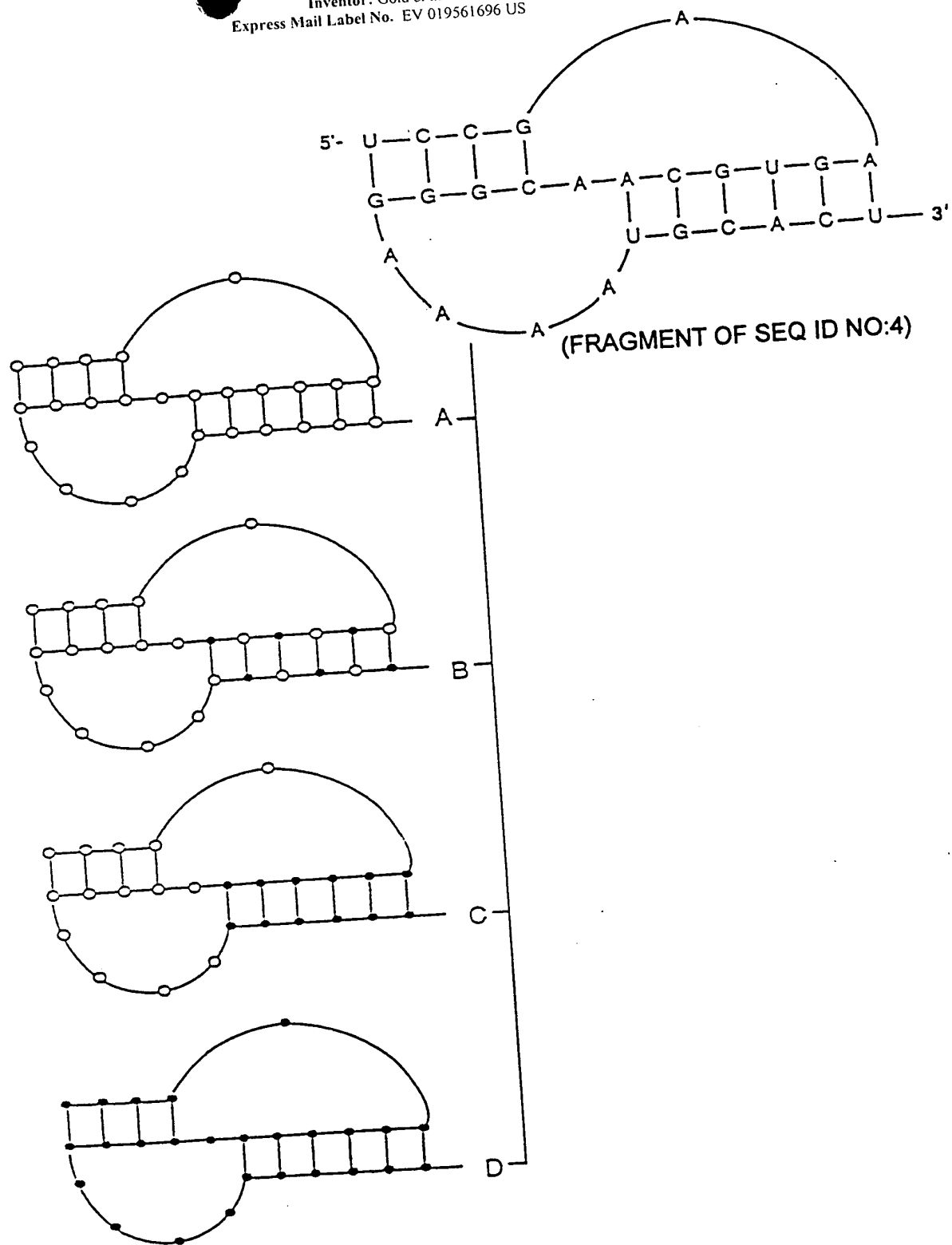


FIG. 6



● : denotes a 2' O-methyl instead of an OH,
 denoted by (○), at this position on the ribose

FIG. 7A

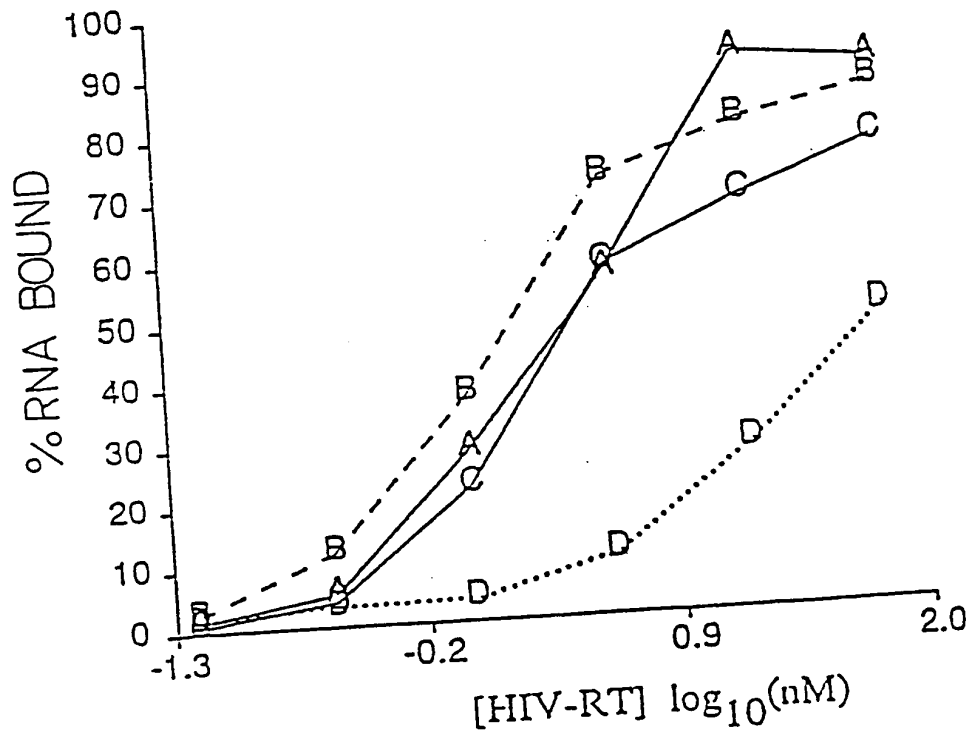


FIG.7B

2010-04-01

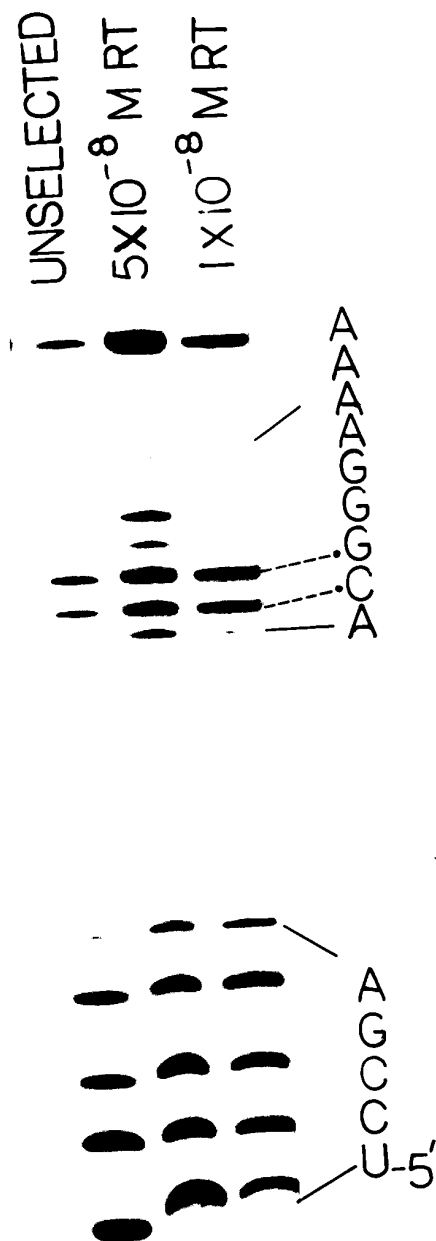


FIG. 8

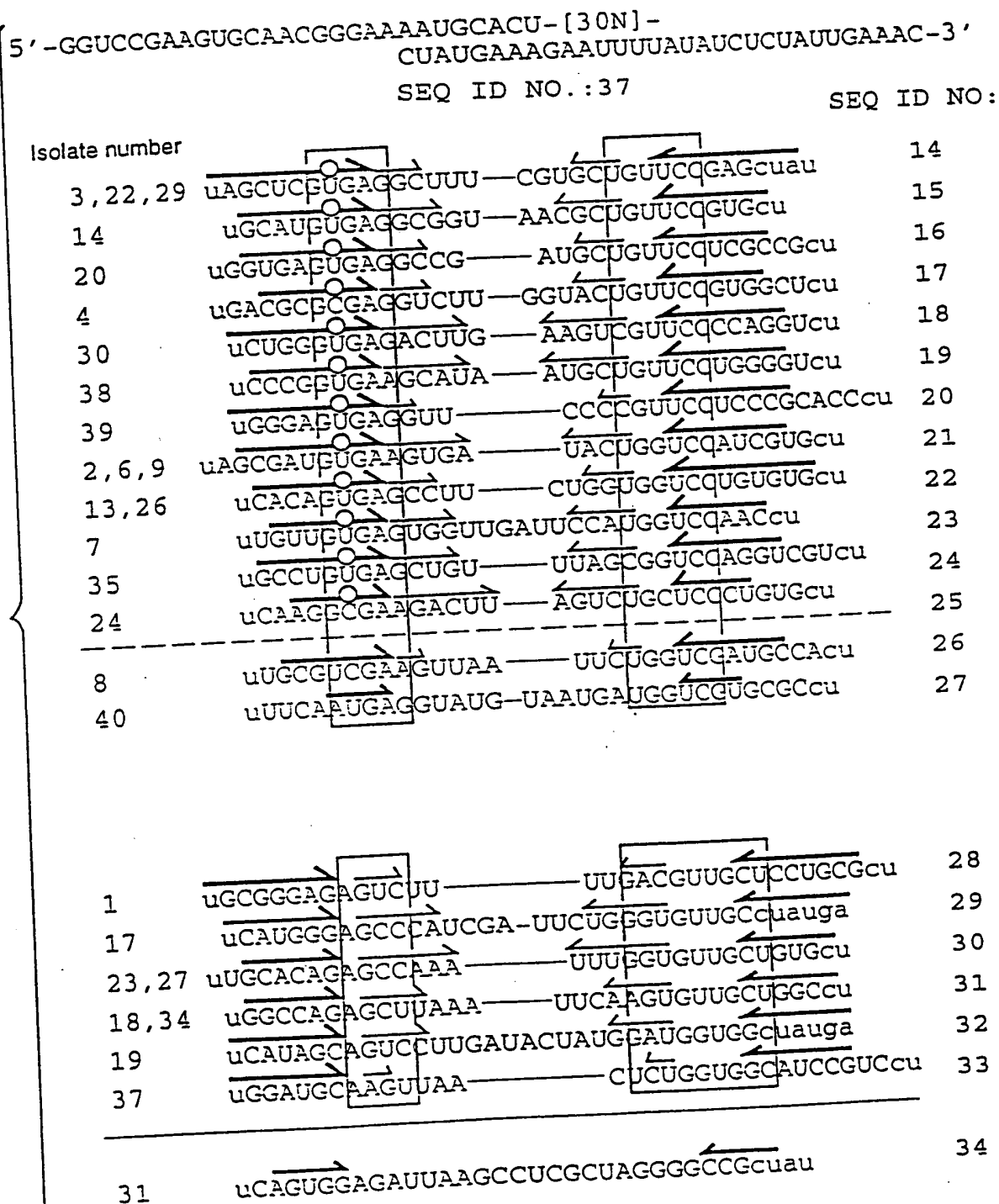


FIG. 9

2004-07-02

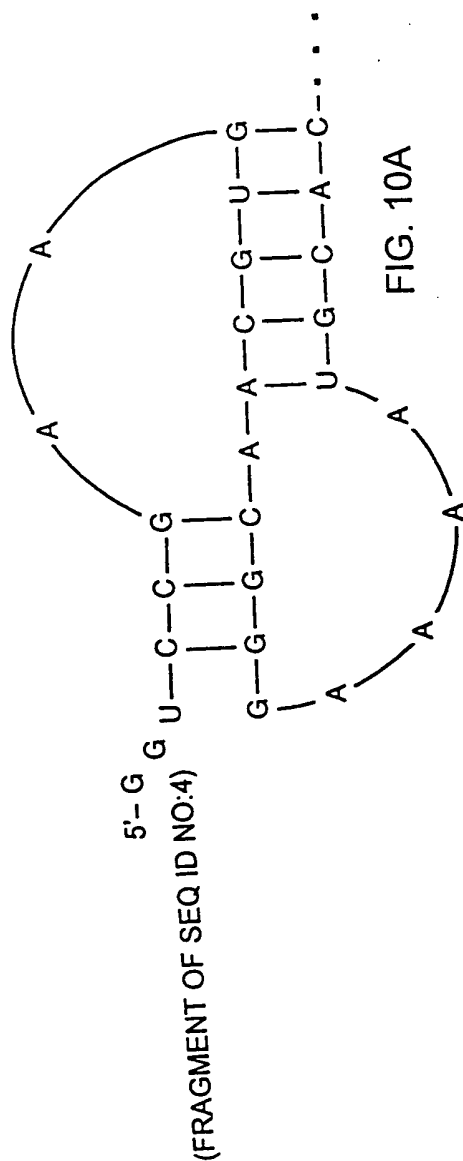


FIG. 10A

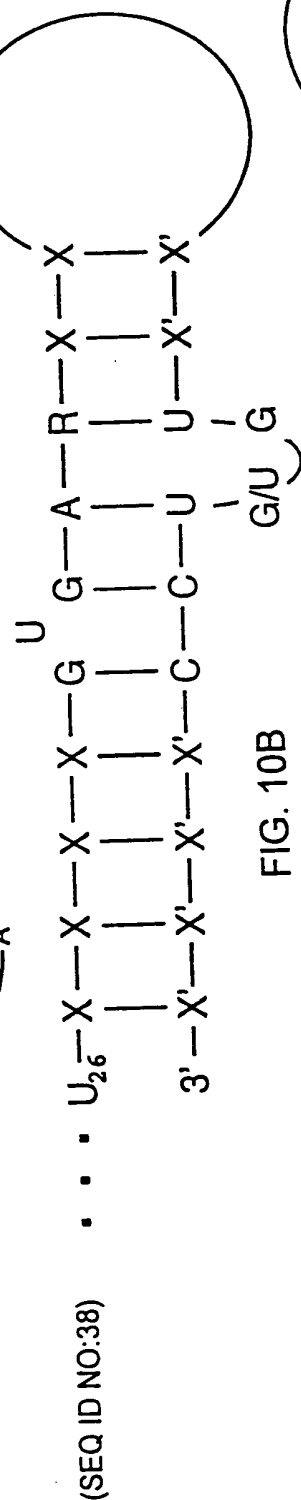


FIG. 10B

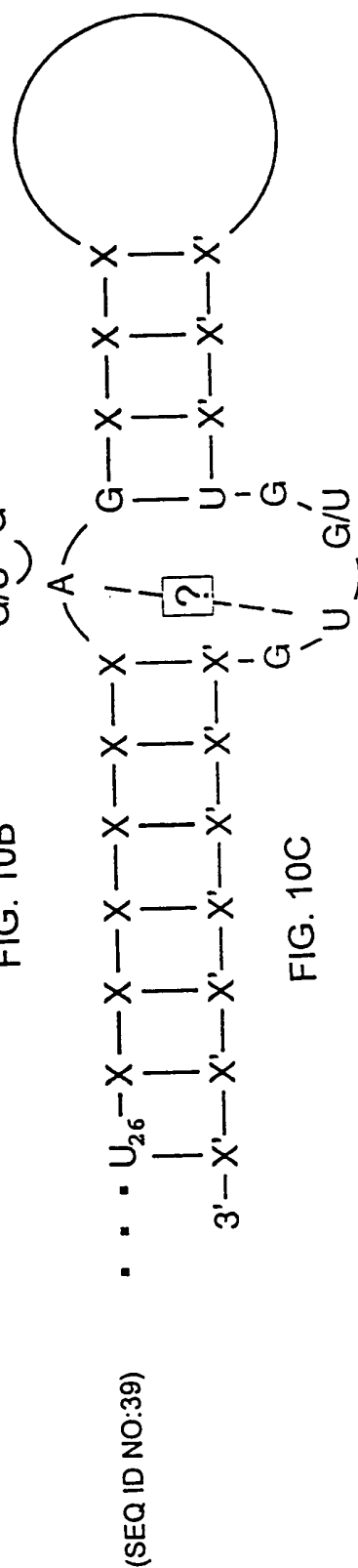


FIG. 10C

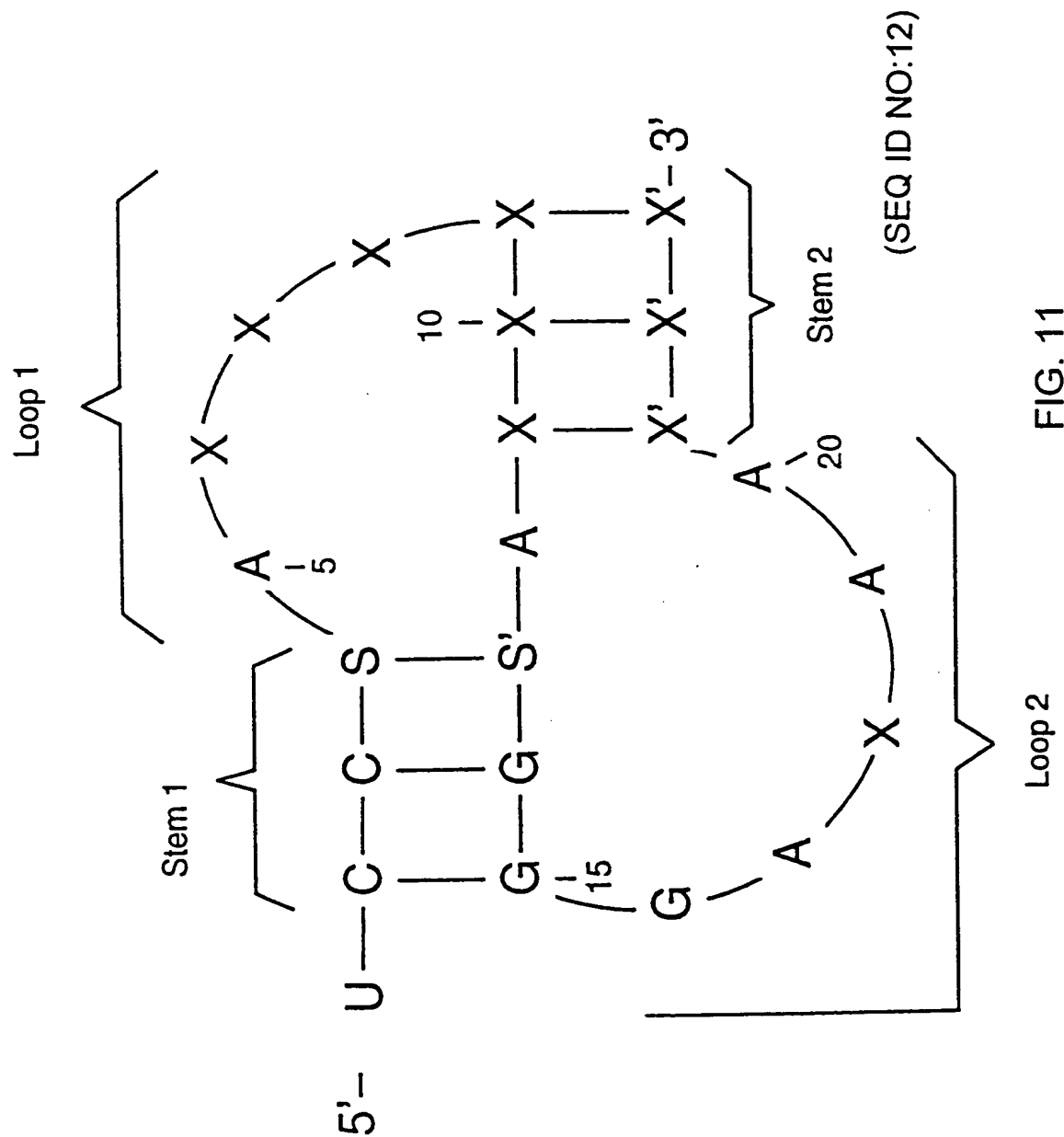


FIG. 11

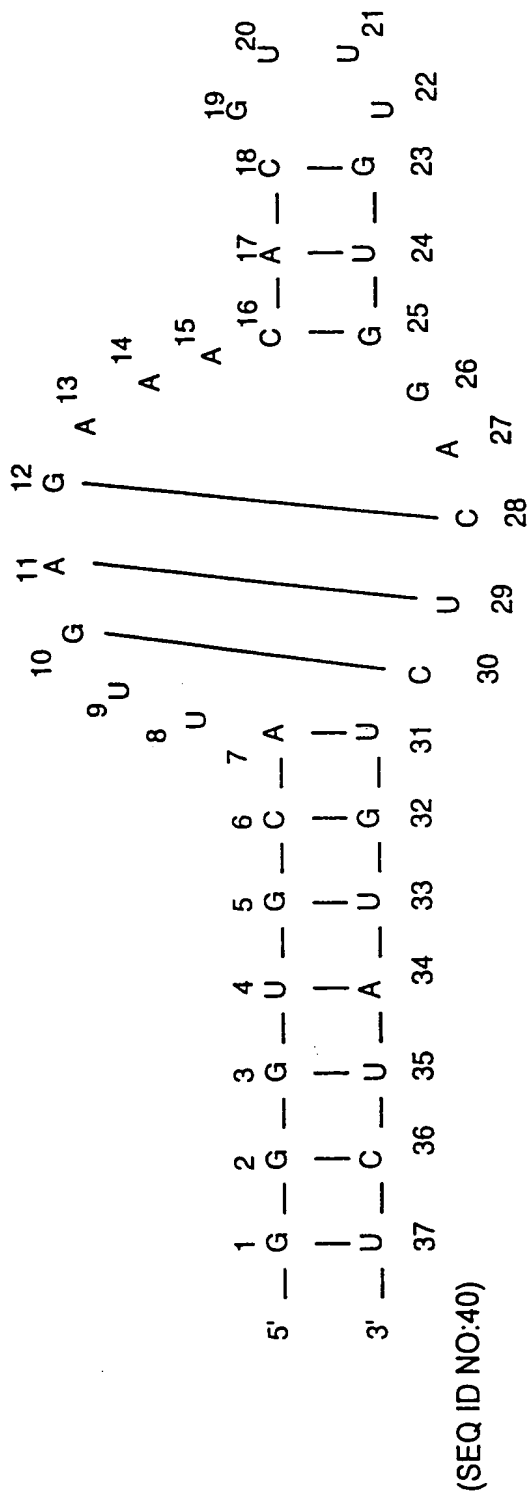


FIG. 12A

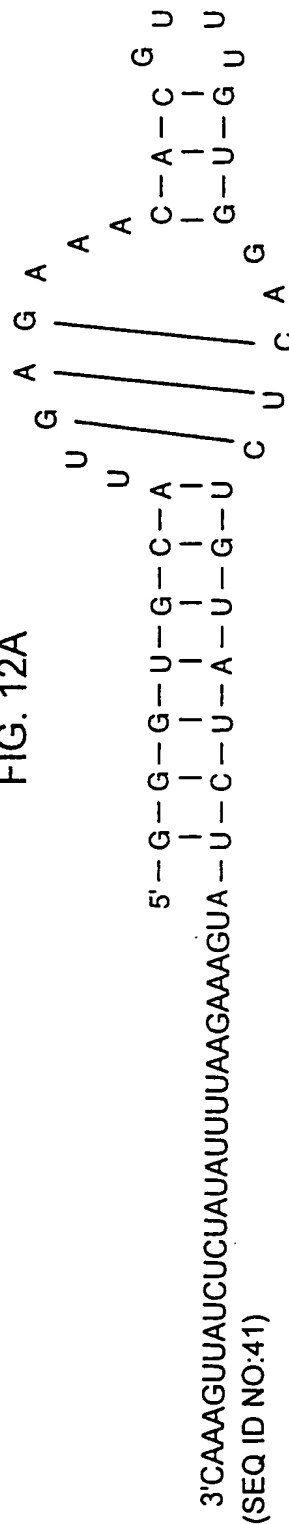














FIG. 12B

(SEQ ID NO:42) 5' GTTCAATAGAGATATAAAATTC 3'

FIG. 12C

modifying agent		partial		full
		less	more	
KETHOXAL	N1G,N2G			
DMS	N3C,N1A			
CMCT	N3U,N1G			
DEPC	N7A,N7G			

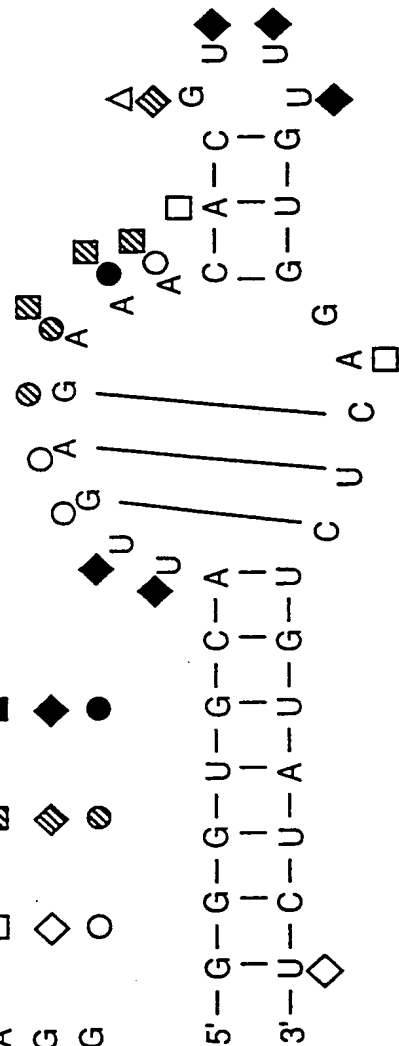


FIG. 13A

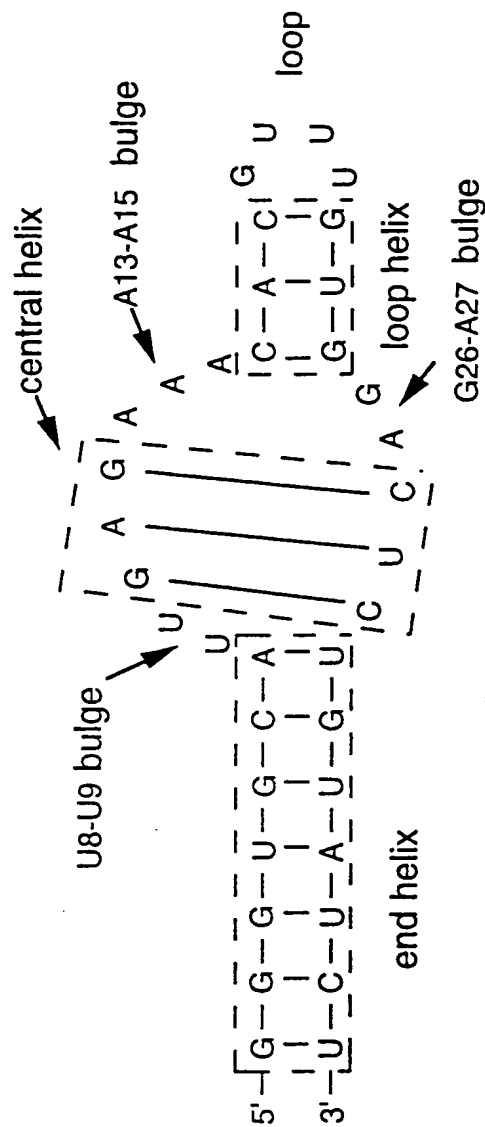


FIG. 13B

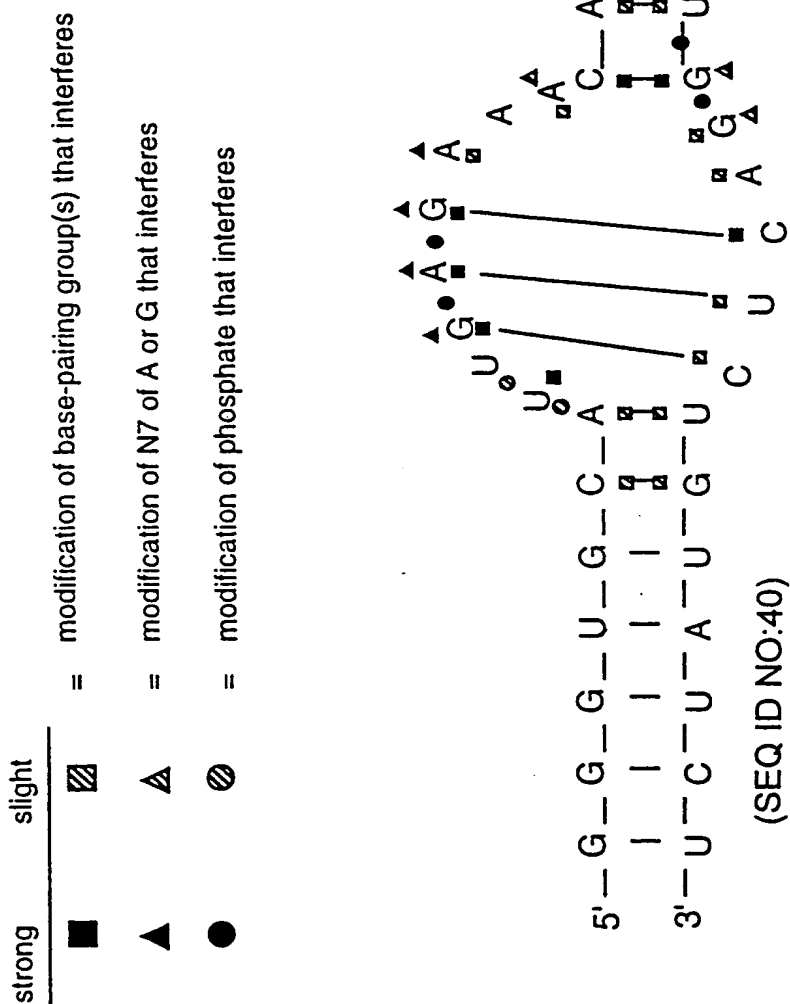


FIG. 14



FIG. 15

202070" 25404007

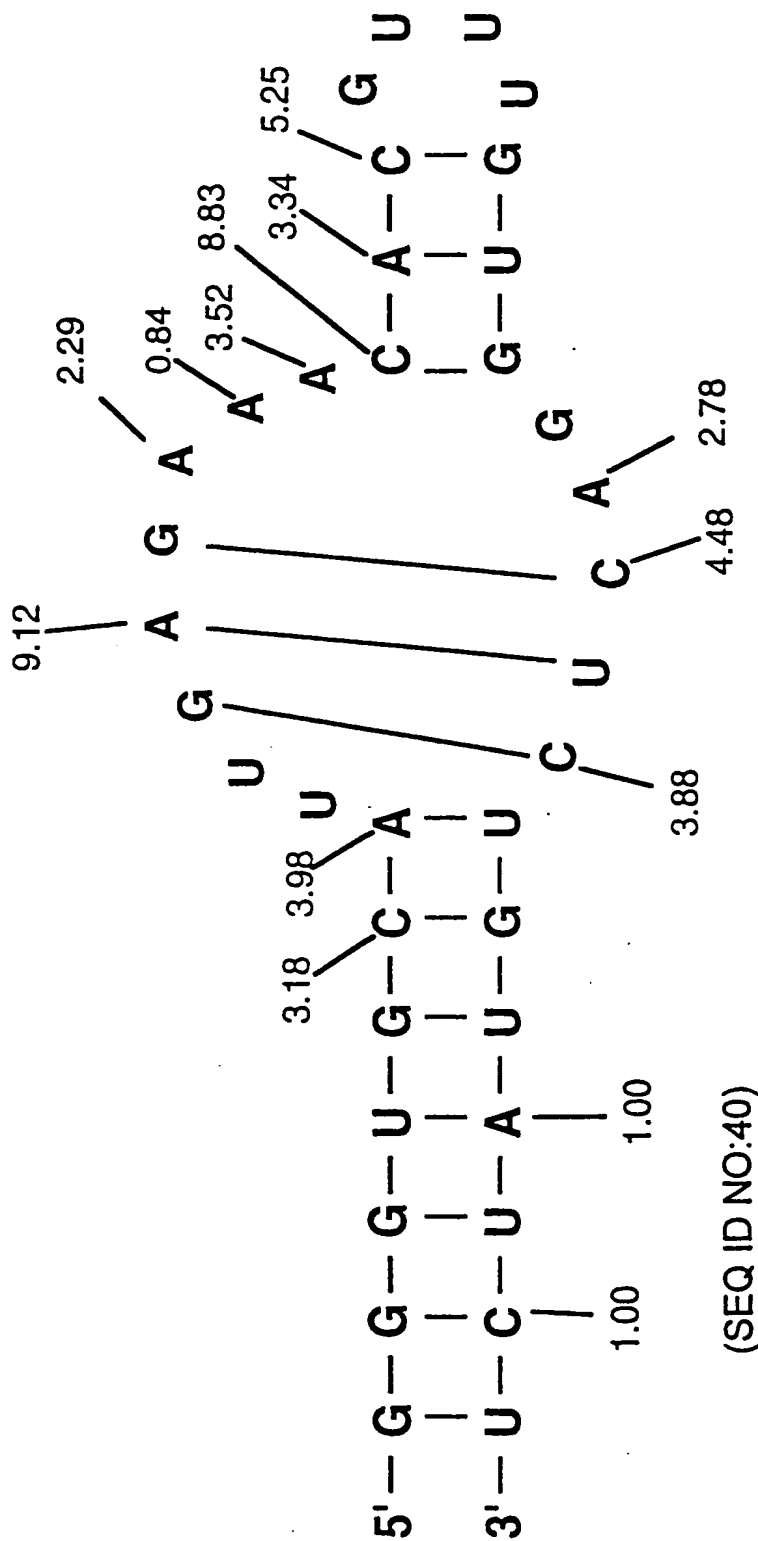


FIG. 16

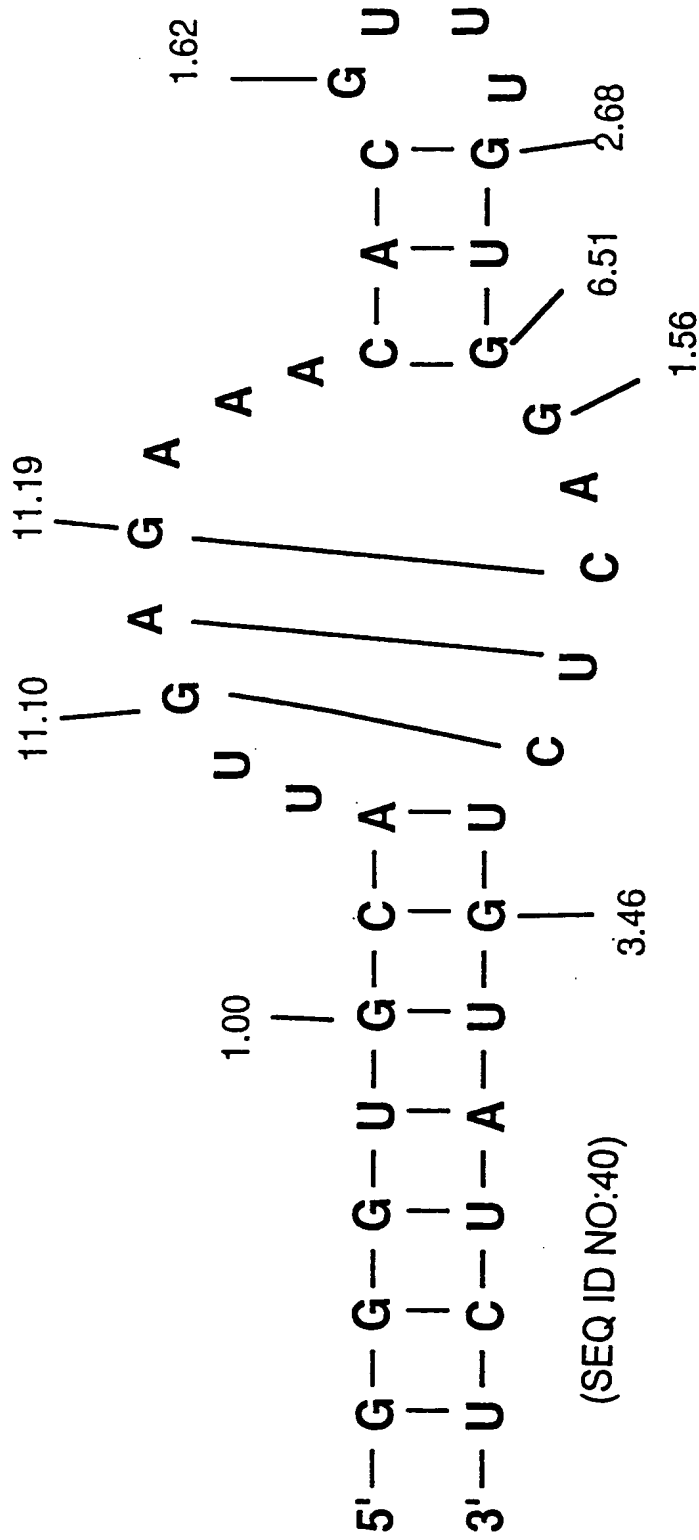
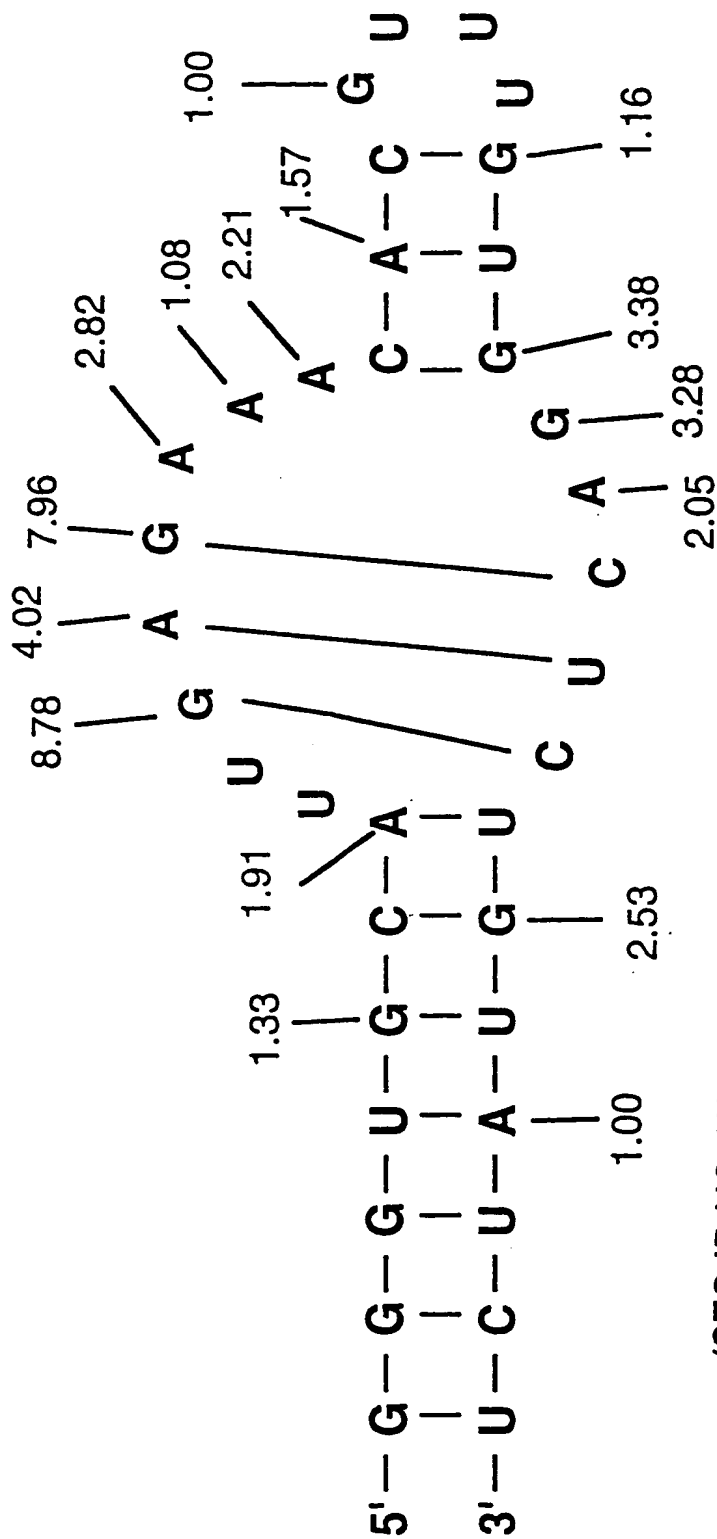


FIG. 17



FIG. 18

202070" 26404007

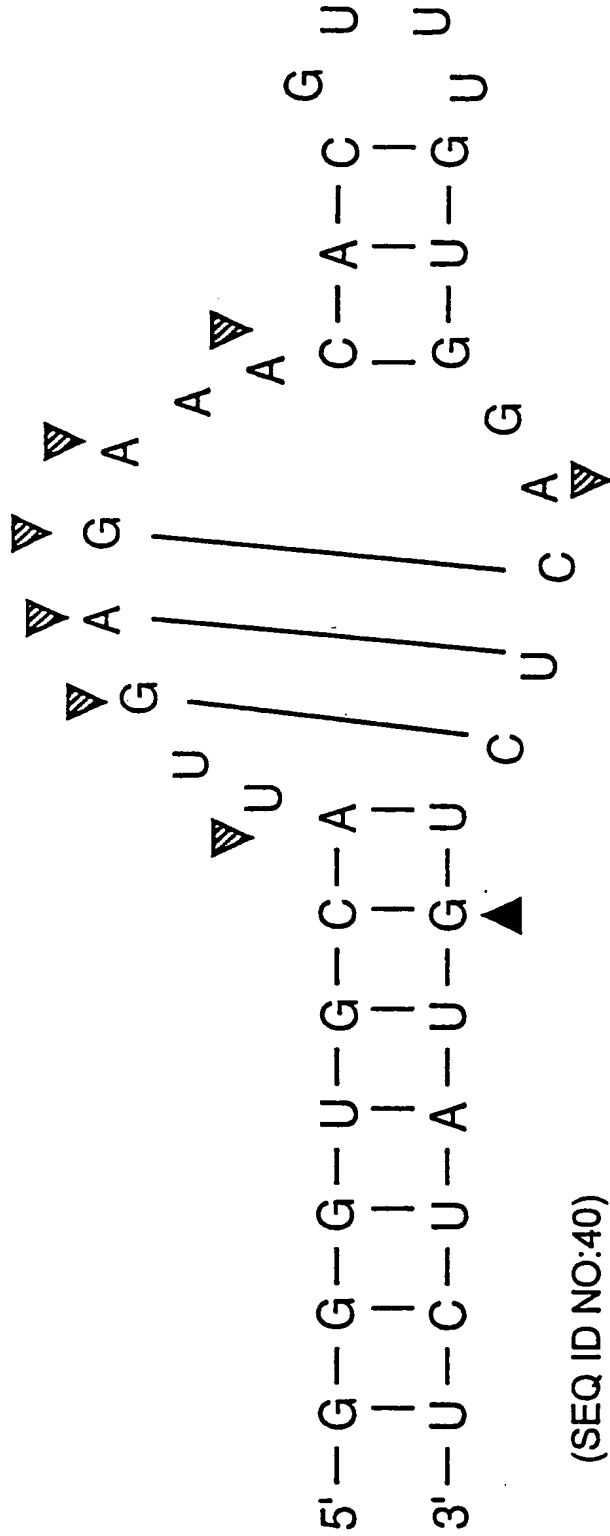


(SEQ ID NO:40)

FIG. 19

202010" 2640000T

▼ = reduced modification of base
▲ = enhanced modification of base



(SEQ ID NO:40)

FIG. 20

		SEQ ID NO.:43	
5'-GGGACUAUUGAUGGCCUCCGACC-6a-CACACAGAGGUAAGAGGAUCCGGG-3'			
Biased ligand sequences		SEQ ID NO.:	
6a	<u>GGGUGCAUUGAGAAACACGU-UUGUGGACUCUGUAUCU</u>	40	
1	<u>DGGUGCGUUGAGAAACAGGU-UUUUGGACUCCGUACCA</u>	45	
2	<u>GUAUGCAUUGAGAGUCACAC-UUGUGGACUCUGCAUCC</u>	46	
3	<u>AGAUGGAUUGAGAAACACUA-UUAUGGACUCUCCAUCC</u>	47	
4	<u>AGCUUCGUGGAGAUACACGU-UGAUGGACUCCGAAGCA</u>	48	
5	<u>UCGUACGUUGAGAAACAAGU-UUAUGGACUCCGUAACCU</u>	49	
6	<u>UCGAUCGUUGAGAUACACGC-UAGUGGACUCCGAAACU</u>	50	
8	<u>UACUGCAUCGAGAUACACGU-UUGUGGACUCUGCACAU</u>	51	
9	<u>UGAUACGUUGAGAAACACAA-UGCUGGACUCGGCAUCC</u>	52	
10	<u>GCCUGCAUUGAGAAACAGGA-UUCUGGACUCUGCCACU</u>	53	
12	<u>CGCUAUGUUGAGAAACACUU-UGCUGGACUCCGUAGCU</u>	54	
13	<u>UACUGCAUCGAGAAACACGU-AAGUG-ACUCUGCAUCC</u>	55	
15	<u>CGGUACGUUGGAGAUACACGA-AGAUGGACUCCGUUAUCC</u>	56	

FIG. 21-A

202070" 2540400F

SEQ ID NO.:

17	<u>AACUCCAUCGAGAGAAACACGA-UAGUGGACUCUGGAGCU</u>	57
18	<u>GGAGACGUCGAGAAACACCGU-UUGUGGACUCCGUCUCU</u>	58
21	<u>AGCUACAUCGAGAGAAACAAGA-UUUVUGGACUCUGUAGCG</u>	59
23	<u>AAGUGCAUUGAGAGUACAATAU-GAUUGGACUCUGGACAC</u>	60
24	<u>UGCUACGUUGAGAGUACAACGU-UGAUGGACUCCGUAGCU</u>	61
25	<u>AGCUACGUUGAGAGUACAACGUUACGUGG-CUCCGUAGCC</u>	62
27	<u>GAGUGGCUCGAGAAACAGGU-UGCUGGACUCGCCACAU</u>	63
28	<u>UCGUGCGUCGAGCAACACCGU-UGAUGGACUCCGCAACG</u>	64
29	<u>GGCACCGUUGAGAGAAACACAU-GCGUGGACUCCGUGCCC</u>	65
30	<u>UCCUGCAUUGAGAGAAACAGUG-AUCUGGACUCUGCAACU</u>	66
31	<u>CUGUGGAUUGAGCAACACCGU-GAGUGGACUCUCCACAU</u>	67
32	<u>CCGUGCGUUGAGACACACAC-CGAUGGACUCCGCAUGU</u>	68
33	<u>AGCUGCAUCGAGAGUACAACGA-UUGUGGACUCUGCAGCC</u>	69
35	<u>AGAUUCGUUGAGAGAAACACAU-GGGUGGACUCUCCCCGUA</u>	70
36	<u>AGAUGGAUUGAGAGAAACACCGU-UCGUGGACUCUCCACAU</u>	71
37	<u>GACUGCAUCGAGAGAAACACUG-AUGUGGCCUCCGCCACGG</u>	72

FIG. 21-B

204010" 4641001

SEQ ID NO.:

38	<u>AGCUACGUUGAGAAACAGUA-UAAUGGACUCCGUAGCU</u>	73
40	<u>GAGUGCGUCGAGAAACACAU-UUGUGGACUCCGCCACAC</u>	74
42	<u>UCGUACGUUGAGAAACACGC-UAGUGGACUCCGUAVGU</u>	75
43	<u>AGAUACGUUGAGAGACACGC-ACGUGGACUCCGUUAUCU</u>	76
44	<u>AGGAUACAGAGAAACACCGUGGGUGG-CUCCCUUAU</u>	77
45	<u>GUGCGCAUCGAGAAACACCGU-UGAUGGACUCUGCAUGCAC</u>	78
47	<u>GAGAGGAUCGAGAAACACCGU-AUGUGGACUCUCCAUUCU</u>	79
48	<u>GGAUGGAUUGAGACACACCGU-AUGUGGACUCUCCAUCA</u>	80
49	<u>UCGGGCAUUGAGAUACACCGU-AGAUGGACUCUGUCUCA</u>	81
50	<u>UGGACCGUAGAGAAACACCGUUUGAUGG-CUCCCUUCUGU</u>	82

FIG. 21-C

202070" 2640400T

6a	G	G	G	U	G	C	A	U	U	G	A	G	A	A	A	C	A	C
wt	10	19	16	30	20	31	18	37	22	38	38	38	36	25	38	38	38	30
Δ	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
A	12	8	8	5	11	0	18	0	2	0	38	0	36	25	38	0	38	3
C	3	8	14	1	3	31	1	1	14	0	0	0	2	2	0	38	0	30
G	10	19	16	2	20	4	19	0	0	38	0	38	0	2	0	0	0	5
U	19	2	0	30	4	1	0	37	22	0	0	0	0	9	0	0	0	0
bp	16	20	26	31	33	35	35			38	38	38				38	38	26

FIG. 22A-1

6a	G	G	G	U	G	C	A	U	U	G	A	G	A	A	A	C	A	C
wt	.26	.50	.42	.79	.53	.82	.47	.97	.58	1.00	1.00	1.00	.95	.66	1.00	1.00	1.00	.79
D	.00	.03	.00	.00	.00	.00	.00	.00	.00	.00	.00	.00	.00	.00	.00	.00	.00	.00
A	.32	.21	.21	.13	.29	.00	.47	.00	.05	.00	1.00	.00	.95	.66	1.00	.00	1.00	.08
C	.08	.21	.37	.03	.08	.82	.03	.03	.37	.00	.00	.00	.05	.05	.00	1.00	.00	.79
G	.26	.50	.42	.05	.53	.11	.50	.00	.00	1.00	.00	1.00	.00	.05	.00	.00	.00	.13
U	.50	.05	.00	.79	.11	.03	.00	.97	.58	.00	.00	.00	.00	.24	.00	.00	.00	.00
bp	.42	.53	.68	.82	.87	.92	.92	.00	.00	1.00	1.00	1.00	.00	.00	.00	1.00	1.00	.68

FIG. 22B-1

204010" 46404000F

G	U	space	U	U	G	U	G	G	A	C	U	C	U	G	U	A	U	C	U
25	22	35	23	14	19	38	38	37	36	38	38	38	17	28	15	31	15	26	19
0	0	35	0	0	0	0	0	1	3	0	0	0	0	0	0	0	0	0	0
7	8	0	9	7	11	0	0	0	36	0	0	0	0	0	2	31	4	7	3
1	5	0	1	4	5	0	0	0	0	38	0	38	20	9	20	6	10	26	11
25	3	0	5	13	19	0	38	37	0	0	0	0	1	28	1	1	9	5	5
5	22	3	23	14	3	38	0	0	0	0	38	0	17	0	15	0	15	0	19
18				18	26	38	38			38	38	38	35	35	33	31	26	20	16



FIG. 22A-2

G	U	space	U	U	G	U	G	G	A	C	U	C	U	G	U	A	U	C	U
.66	.58	.92	.61	.37	.50	1.00	1.00	.97	.95	1.00	1.00	1.00	.45	.74	.39	.82	.39	.68	.50
.00	.00	.92	.00	.00	.00	.00	.00	.03	.08	.00	.00	.00	.00	.00	.00	.00	.00	.00	.00
.18	.21	.00	.24	.18	.29	.00	.00	.00	.95	.00	.00	.00	.00	.00	.05	.82	.11	.18	.08
.03	.13	.00	.03	.11	.13	.00	.00	.00	.00	1.00	.00	1.00	.53	.24	.53	.16	.26	.68	.29
.66	.08	.00	.13	.34	.50	.00	1.00	.97	.00	.00	.00	.00	.03	.74	.03	.03	.24	.13	.13
.13	.58	.08	.61	.37	.08	1.00	.00	.00	.00	.00	1.00	.00	.45	.00	.39	.00	.39	.00	.50
.47	.00	.00	.00	.47	.68	1.00	1.00	.00	.00	1.00	1.00	1.00	.92	.92	.87	.82	.68	.53	.42



FIG. 22B-2

6a	G	G	G	U	G	C	A	U	U	G	A	G	A	A	A	C	A	C
wt	-.37	-.13	-.21	.16	-.10	.19	-.16	.34	-.05	.37	.37	.37	.32	.03	.37	.37	.37	.16
A	.19	.09	.09	.01	.16	-.13	-.16	-.13	-.07	-.13	.37	-.13	.32	.03	.37	-.13	.37	-.05
C	-.05	.09	.24	-.09	-.05	.19	-.10	-.10	.24	-.13	-.13	-.13	-.07	-.07	-.13	.37	-.13	.16
G	-.37	-.13	-.21	-.07	-.10	-.02	.38	-.13	-.13	.37	-.13	.37	-.13	-.07	-.13	-.13	-.13	.01
U	.38	-.07	-.13	.16	-.02	-.10	-.13	.34	-.05	-.13	-.13	-.13	-.13	.11	-.13	-.13	-.13	-.13



FIG. 22C-1

202070" 25707007

G	U	space	U	U	G	U	G	A	C	U	C	U	G	U	A	U	C	U
.03	-.05		-.02	-.26	-.13	.37	.34	.32	.37	.37	.37	-.18	.11	-.24	.19	-.24	.05	-.13
.06	.09		.11	.06	.16	-.13	-.13	.32	-.13	-.13	-.13	-.13	-.13	-.07	.19	-.02	.06	-.05
-.10	.01		-.10	-.02	.01	-.13	-.13	-.13	.37	-.13	.37	.40	.11	.40	.03	.14	.05	.16
.03	-.05		.01	.22	-.13	-.13	.34	-.13	-.13	-.13	-.13	-.10	.11	-.10	-.10	.11	.01	.01
.01	-.05		-.02	.26	-.05	.37	-.13	-.13	-.13	.37	-.13	.11	-.13	-.24	-.13	-.24	-.13	-.13



FIG. 22C-2

202070" 4640400F

6a	G1/U37	G2/C36	G3/U35	U4/A34	G5/U33	C6/G32	A7/U31	C16/G25	A17/U24	C18/G23	G19/U22
WT	2	16	8	28	2	28	16	38	38	19	9
AU	6	0	6	0	10	0	16	0	38	0	2
UA	2	1	0	28	2	0	0	0	0	2	1
CC	5	16	7	2	18	6	18	0	0	3	3
CG	1	2	8	0	1	28	1	38	0	19	1
GU	1	1	8	0	2	0	1	0	0	1	9
UG	4	1	0	0	0	1	0	0	0	0	0
AC	3	3	0	2	1	0	2	0	0	0	1
CA	1	1	2	0	0	0	0	0	0	9	0
other	16	13	7	8	2	3	0	0	0	4	14

FIG. 23A

6a	G1/U37	G2/C36	G3/U35	U4/A34	G5/U33	C6/G32	A7/U31	C16/G25	A17/U24	C18/G23	G19/U22
WT	.05	.42	.21	.74	.05	.74	.42	1.00	1.00	.50	.24
AU	.16	.00	.16	.00	.26	.00	.42	.00	1.00	.00	.05
UA	.05	.03	.00	.74	.05	.00	.00	.00	.00	.05	.03
CC	.13	.42	.18	.05	.47	.16	.47	.00	.00	.08	.08
CG	.03	.05	.21	.00	.03	.74	.03	1.00	.00	.50	.03
GU	.03	.03	.21	.00	.05	.00	.03	.00	.00	.03	.24
UG	.11	.03	.00	.00	.00	.03	.00	.00	.00	.00	.00
AC	.08	.08	.00	.05	.03	.00	.05	.00	.00	.00	.03
CA	.03	.03	.05	.00	.00	.00	.00	.00	.00	.24	.00
other	.42	.34	.18	.21	.05	.08	.00	.00	.00	.11	.37

FIG. 23B

202070" 26404007

6a	G1/U37	G2/C36	G3/U35	U4/A34	G5/U33	C6/G32	A7/U31	C16/G25	A17/U24	C18/G23	G19/U22
WT	-.34	.03	-.18	.35	-.34	.35	.03	.61	.61	.11	-.15
AU	.08	-.02	.08	-.02	.19	-.02	.03	-.02	.61	-.02	-.03
UA	.04	.01	-.02	.35	.04	-.02	-.02	-.02	-.02	.04	.01
GC	.05	.03	.11	.04	.40	.14	.46	-.02	-.02	.06	.00
CG	.01	.04	.19	-.02	.01	.35	.01	.61	-.02	.11	.01
GU	-.34	-.05	-.18	-.02	-.34	-.02	-.05	-.02	-.08	.01	-.15
UG	.09	.01	-.02	-.08	-.02	-.05	-.02	-.08	-.02	-.08	-.02
AC	.06	.00	-.02	.04	.01	-.02	-.03	-.02	-.08	-.02	.01
CA	.01	.01	.04	-.08	-.02	-.08	-.02	-.08	-.02	.16	-.02
other	.17	.09	-.07	-.04	-.20	-.17	-.25	-.25	-.25	-.15	.12

FIG. 23C

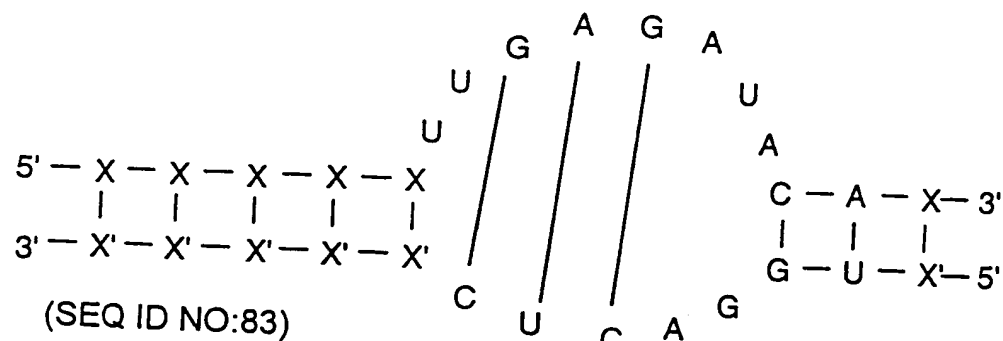


FIG. 24A

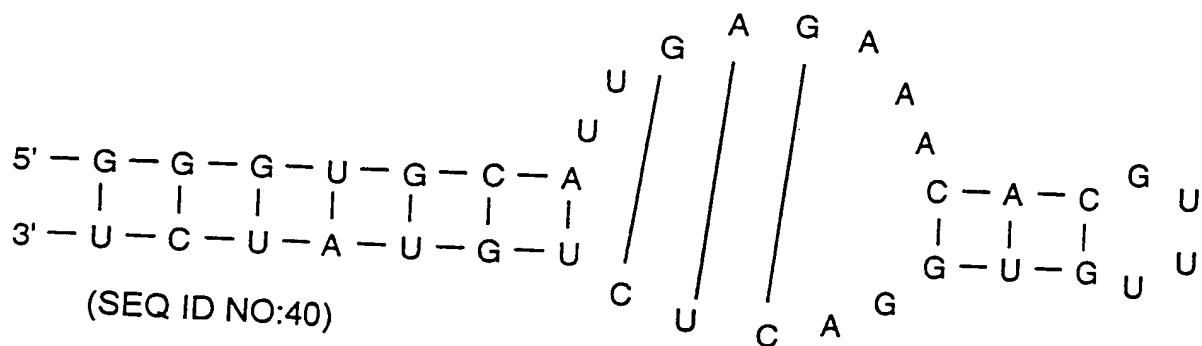


FIG. 24B

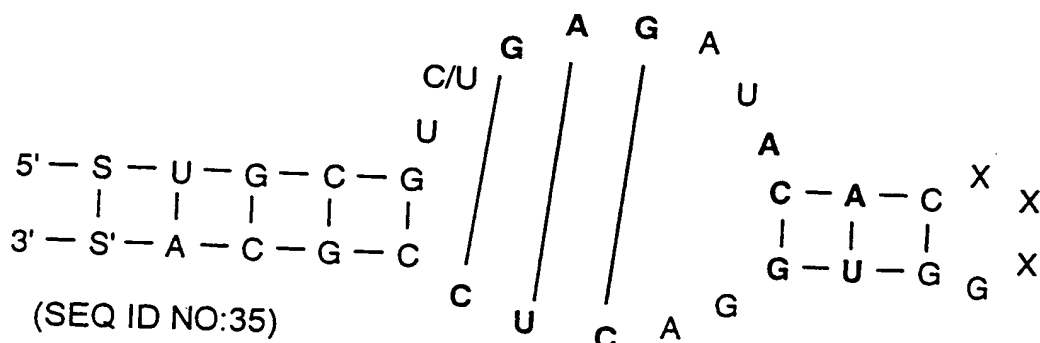


FIG. 24C

202070-26404007